REMARKS

Claims 1-10, 15 and 18-27 are pending in the present application. Claims 7 and 18-27 have been withdrawn from consideration. By virtue of this response, claim 10 has been cancelled; claim 1 has been amended; and new claims 28-37 have been added. Accordingly, claims 1-6, 8, 9, 15, and 28-37 are currently under consideration. Support for the amendment to claim 1 is found on page 3, lines 5-6 of the specification. Support for new claim 28 is found on page 22, lines 6-7 of the specification. Support for new claims 29-37 is found in the specification, *inter alia*, on page 10, line 21 to page 11, line 2. The specification is amended to correct typographical errors. Accordingly, no new matter has been added.

With respect to all claim amendments and cancellations, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional application.

Rejections under 35 USC §112

Claim 10 stands rejected under 35 USC § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons set forth in the Office Action mailed on 03/26/05.

Without acquiescing to the rejection, Applicants respectfully note that claim 10 has been canceled. Thus, this rejection becomes moot. Applicants respectfully request that the rejection be withdrawn.

Claims 1-6, 8-10 and 15 are rejected under 35 USC § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, has possession of the claimed invention. The Examiner states that the specification does

not provide a written description of the phrase "and the cells are introduced in the mammal without adjuvant" as recited in the claims. The Examiner concludes that such limitations recited in the present claims, which did not appear in the specification as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. §112.

Applicants respectfully traverse this rejection. Applicants refer the Examiner to Example 2 on page 22, lines 6-7 of the specification. The specification specifically states that "mice were immunized with $5x10^6$ intact BUD or RED cells, without adjuvant, weekly for 10 to 15 weeks" (emphasis added). In light of the foregoing, Applicants submit that the limitation of "without adjuvant" recited in the claims is well supported in the specification as filed and does not introduce new concepts. Applicants therefore respectfully request the withdrawal of this rejection.

Claim 10 stands rejected under the second paragraph of 35 USC § 112 for allegedly being indefinite in the recitation of ASC, ESC, ROG, BUD, RED, NODD, BR516, RL-65 and NEP because their characteristics are not known.

Without acquiescence to the rejection, Applicants note that claim 10 has been canceled. Thus, this rejection is rendered moot. Applicants respectfully request that the rejection be withdrawn.

In view of the above, Applicants respectfully request that rejections under 35 U.S.C. §112 be withdrawn.

Rejections under 35 USC §103(a)

Claims 1-6, 8-10 and 15 stand rejected under 35 USC § 103(a) as allegedly being unpatentable over Okabe (Cancer Res., 1984, 44:5273-5278, IDS reference 37, of record) in view of Mather et al. (U.S. Patent No. 5,364,785 IDS reference 1, of record) for the reasons set forth in the Office Action mailed 03/25/05. The Examiner further states that the lack of experimental details is not the confirmation that the adjuvant was used in Okabe et al. especially in the absence of the

contrary. The Examiner states that the adaptation of serum free media was taught in Mather et al., and therefore the combination of the teachings remain obvious.

Applicants respectfully traverse this rejection.

The claims of the present invention are directed to methods of using viable and intact cells of a specific cell type and/or cultured cells as an immunogen to immunize a host mammal to produce a population of monoclonal antibodies that bind to antigens representative of a specific cell type that are heterologous to the host mammal, wherein the surface of the cells are free of serum and the cells that are introduced into the mammal are prepared under conditions that maximize the preservation of intact antigens, especially cell surface antigens.

Okabe et al. do not teach or suggest using viable and intact cells of a specific cell type as immunogen to immunize a host mammal. Okabe et al. do not produce a population of monoclonal antibodies that bind to antigens representative of a specific cell type that are heterologous to the host mammal. Okabe et al. do not prepare an immunogen wherein the surfaces of the immunizing cells are free of serum. What Okabe et al. do teach is the production of antibodies by immunizing with minced small cell carcinoma tumors (see page 5273, column 2) that have been maintained in BALB/c nude mice. These tumors are neither of a specific cell type nor are they a homogeneous population of cells. Minced tumors as used by Okabe et al., are commonly made up of a heterogeneous population of cells (tumor, stromal, endothelial, etc.). This heterogeneity is exacerbated by Okabe et al. when they maintain their minced tumors in BALB/c nude mice instead of in defined culture conditions as taught in the present application. Okabe et al. do not teach the purification of the small cell carcinoma cells (the desired immunogen) from the infiltrating cells of the host mouse. Because Okabe et al. only teach injecting minced tumors, which commonly contain a mixed population of cells, Okabe et al. do not provide the motivation for one skilled in the art to use viable and intact cells of a specific cell type as an immunogen.

The missing teachings are not provided by Mather et al. Mather et al. teach maintenance of rat epithelial cells in serum-free culture and do not teach or suggest using these cultured cells as

immunogens to generate a population of monoclonal antibodies that bind to antigens representative of a specific cell type. One skilled in the art would not be motivated to combine the referenced teachings to arrive at the claimed invention.

Additionally, the cited references do not teach (as is stressed in the pending application) the importance of preserving the native conformation of cell surface proteins. The present application, not the cited references, discloses precautionary methods such as serum-free culture conditions to maintain membrane integrity and to preserve cell membrane components when harvesting cultured cells for immunization. Also, as noted above, Example 2 of the specification teaches the introduction of a specific population cells into BALB/c mice without the use of adjuvant. The use of adjuvant would result in the destruction of the integrity of cell membrane components and alters the native conformation of cell surface antigens.

Applicants' position is that Okabe el al. do not disclose immunizing mice without adjuvant. The lack of experimental details in Okabe et al. would indicate to one skilled in the art that a standard protocol was used, although Okabe et al. do not specifically address the use of adjuvant. As pointed out in the Mather Declaration submitted in the previous response, the conventional protocol at the time of the publication uses Freund's adjuvant in immunizations. Mather et al. do not disclose methods of immunization without adjuvant.

The references cited by the Examiner, even if combined, neither teach nor suggest immunization methods that maximize the preservation of intact antigens as are taught in the claimed invention. The immunization methods taught by Okabe et al. do not address the preservation of the native conformation of cell surface components. Such methods were not taught nor suggested in the Okabe reference. Similarly, Mather et al. do not disclose methods of immunization using cells prepared under conditions to maximize the preservation of intact antigens nor do they perform any immunizations. Accordingly, the references cited by the Examiner, alone or in combination, do not

teach or suggest all the claim limitations and provide no motivation to combine the referenced teachings.

In light of the foregoing amendment and remarks, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness. Withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. **415072000101**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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